Remote Enzyme Catalysis: Coupling Long Range Electron Transfer to Radical-Mediated Chemistry

The tryptophan tryptophylquinone (TTQ) cofactor of methylamine dehydrogenase (MADH) is a catalytic and redox center formed by posttranslational modifications of two otherwise inert tryptophan residues. This process is an 8-electron oxidation that requires insertion of an oxygen into the indole ring of a tryptophan, crosslinking the modified indole ring to that of another tryptophan residue, insertion of a second oxygen into the tryptophan side chain, and oxidation of the resulting quinol to TTQ. The initial oxygenation is an autocatalytic reaction. The subsequent three 2-electron oxidation reactions are catalyzed by the diheme enzyme, MauG. During these reactions, MauG cycles through a unique \( \text{bis-Fe}^{IV} \) intermediate with one heme as \( \text{Fe}^{IV} = \text{O} \) and the other as \( \text{Fe}^{IV} \) with the two axial ligands provided by histidine and tyrosine residues. The crystal structure of the MauG-preMADH complex reveals that the heme irons of MauG are located 19 and 40 Å from the site on the surface at which the MADH precursor binds. Thus, catalysis does not involve direct contact between the protein substrate and either heme. Instead, MauG performs remote catalysis using a hole-hopping mechanism of electron transfer in which specific intervening amino acid residues of MauG are reversibly oxidized. In this manner, long range electron transfer is efficiently coupled to the radical-mediated chemical reactions that are required for TTQ biosynthesis. If the \( \text{bis-Fe}^{IV} \) intermediate is generated in the absence of the substrate, it is unusually stable but eventual oxidizes specific methionine residues on MauG, thus inactivating itself. The unusual mechanisms by which the catalytic and self-inactivating reactions occur, and the implications of these results will be discussed.

Prof. Victor Davidson

Burnett School of Biomedical Sciences
University of Central Florida

Wednesday, October 31, 2018

3:30pm in room 1315 Chemistry

If you wish more information please call 262-6815
Refreshments will be available at 3:15 pm outside of Seminar Hall